PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION REGARDING REVIEW OF JUSTIFICATION FOR INVITATION TO PAY ADDITIONAL SEARCH FEES

(PCT Rule 40.2(e))

REGISTERED MAIL

To:
ISENBRUCK BÖSL HÖRSCHLER
WICHMANN HUHN
Attn. Wichmann, Hendrik
Prinzregentenstrasse 68
D-81675 München
GERMANY

Isenbruck | Bösl | Hörschler | Wichmann | Huhn, Patentanwälte
Postfach 860880
D-81635 München

30. Nov. 2004

FEES

Frist: 26. 12. 04
Vorfrist: 16. 12. 04
WV

Date of mailing *(day/month/year)*	26/11/2004	B1	HJW
PAYMENT DUE	**ONLY** if item 1 applies: within **ONE MONTH** from the above date of mailing	B2	
		B3	
International filing date *(day/month/year)*	14/05/2004	Sekr	HG
		EDV	
		Ablg.	

Applicant's or agent's file reference
C62780PC

International application No.
PCT/EP2004/005208

Applicant
CYTOS BIOTECHNOLOGY AG

1. [x] The applicant is hereby notified that, with regard to the protest filed on 20/09/2004, this International Searching Authority has reviewed the justification for the invitation to pay additional search fees (Form PCT/ISA/206) and the applicant is invited to pay a protest fee, within the time limit indicated above, for further examination of the protest, in the amount of

_____ *(currency/amount)*

or, EUR 1.020,00

because [x] the invitation is justified.

[ ] the invitation is justified in part.
To the extent the invitation is not justified, _____ additional search fee(s) paid under protest will be refunded in due course.

The reasons for this invitation to pay a protest fee are indicated in the Annex.

Failure to pay the protest fee within the time limit indicated above will result in the protest being considered withdrawn.

2. [ ] The applicant is hereby notified that, with regard to the protest filed on _____, this International Searching Authority has reviewed the justification for the invitation to pay additional search fees (Form PCT/ISA/206) and has found that the invitation was not justified.
Any additional search fee(s) paid under protest will be refunded in due course.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Anna Rauf

Form PCT/ISA/228 (January 1994)

Application number: EP2004/005208

Internal Notes

Result of the Prior Review according to Rule 40.2(e) PCT for EP0405208

The objection under lack of unity raised in the ISR is maintained for the following reasons:

The requirements of unity of invention (Rule 13 PCT) are not fulfilled in that there is no technical relationship among the inventions as they do not involve one or more of the same or corresponding special technical features.

Claim 1 refers to a method for selecting at least one antigen-specific B cell from a mixture of cells comprising: a mixture of cells comprising B cells, a first composition comprising a core particle, at least one antigen, wherein the antigen and the core particle form through association an ordered and repetitive antigen array, contacting the first composition with said mixture of cells, labelling the composition and the B cells independently and selecting a B cell which is positive for said first and second labelling compound. Claim 2, refers to the different core particles used: a virus, a virus-like particle, a bacteriophage, a bacterial pilus, a viral capsid particle and a virus-like particle of a RNA-phage. According to Rule 13 PCT a group of inventions is considered to be unitary only if so linked as to form a single general inventive concept. The sole concept linking independent claim 1 and the different core particles of claim 2 is the use of said core particles for the isolation of antigen-specific B-cells by forming an ordered and repetitive antigen array. However, the use of virus-like particles for the isolation of antigen-specific B-cells is already known in the art.
Thus, in the light of the prior art, the problem to be solved by the present application can be formulated as follows: How to isolate further antigen-specific B-cells by core particles forming an ordered and repetitive antigen array. The solution to this problem is a composition comprising a core particle and an antigen according to present claim 1.
However, the use of a Rotavirus derived virus-like particle for the isolation of Rotavirus-specific B-cells is known from the prior art (see J. Immunol. Methods (D1)*, vol. 275, 2003, pg.: 223-237, abstract, page 224, col. 2, second para. to page 225, col. 1, para. 1, figure 1; page 235, col. 1, third para. to page 236, col. 1, second para.). Moreover, the Review Board is of the opinion that D1 is also detrimental to the concept of an ordered antigenic composition array as referred to in claim 1 for the following reasons:
Claim 1 refers broadly to a composition comprising a "core particle" and an antigen. D1 discloses on page 224, second col., second paragraph that the RV virus-like particle consists of recombinantly produced proteins VP2, VP6 and VP7 wherein VP6 and VP7 are

 * Weitkamp et al. 2003

Application number: EP2004/005208

strongly antigenic in contrast to VP2. VP2 must therefore be covered by the two other antigenic proteins meaning that it acts as a "core or nucleation particle" for the two other antigens. The Review Board would like to point out that neither the term "core particle" nor the term "antigen" is defined in claim 1 and have therefore to be broadly interpreted. Thus, the RV VLPs of D1 are at the same time "core particles" according to claim 2 as well as a composition according to claim 1 forming a highly repetitive antigenic structure comprising a core particle and an antigen. Additionally, the application itself uses a Hepatitis B core antigen being a single protein as a "core particle" (see example 1 of the present application). All the other method steps of claim 1 are disclosed in D1 starting from page 225 fig. 1 and col. 2, second para. to page 226, col. 1, last para.). Thus, D1 is clearly detrimental to the novelty of the concept of present claim 1. Consequently, all the other core particles mentioned in claim 2 constitute separate alternative solutions to the problem mentioned above. Thus, there is no longer a technical relationship between the six core particles mentioned above.

Consequently, the lack of unity objection is upheld and neither refund of the additional search fee can be granted nor the search over the whole ambit as requested by the applicant in his letter of 20.09.2004. An additional search will be carried out for the group 6 invention as requested.

G. Hillenbrand M. Montrone B. Isert